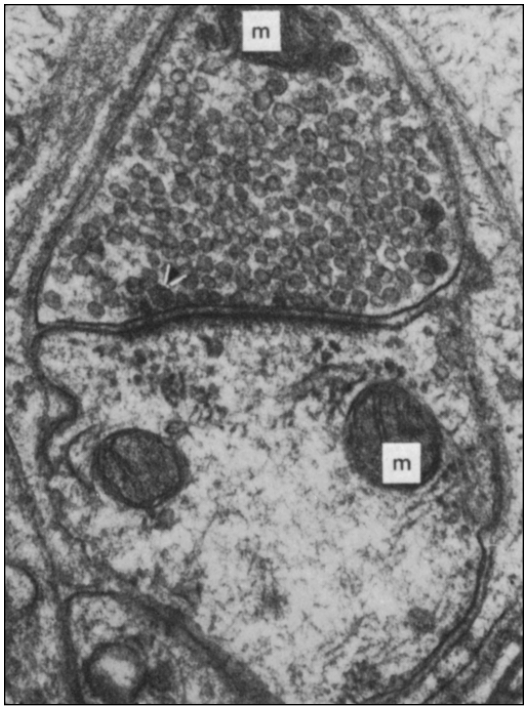
Lesson 3
Explain/ Elaborate

Drugs Change the Way Neurons Communicate



From: *Principles of Neural Science*, Third edition, Eric R. Kandel, James H. Schwartz, Thomas M. Jessell ©The McGraw-Hill Companies. (m = mitochondria)

At a Glance

Overview
Students build upon their understanding of neurotransmission by learning how different drugs of abuse disrupt communication between neurons. Students then conduct an activity investigating the effect of caffeine on their heart rate. Finally, students analyze data on how the way a drug is taken into the body influences its effect.

Major Concept
Drugs affect the biology and chemistry of the brain.

Objectives
By the end of these activities, the students will

- understand that certain drugs interfere selectively with neurotransmission, and
- realize that the effect of a drug is dependent upon dosage and route of administration.

Basic Science–Health Connection
Drugs of abuse are valuable tools for investigations of brain function because they can mimic or block actions of neurotransmitters, and thus exert effects on homeostasis and behavior.

Background Information

Drugs Disrupt Neurotransmission

How do drugs cause their effects on the brain and behavior? Lesson 1 introduced students to the idea that a specific brain region, the reward system (part of the limbic system), regulates feelings of pleasure and that this region is activated by drugs of abuse. But what do drugs actually do in that brain region? Drugs interfere with neurotransmission. More specifically, drugs of abuse produce feelings of pleasure by altering neurotransmission by neurons in the reward system that release the neurotransmitter dopamine.[1,2] Thus, drugs of abuse alter the communication between neurons that is mediated by dopamine. Because the synapse is so complex, there are a variety of sites at which drugs may affect synaptic transmission. One way to affect synaptic transmission is to increase the amount of neurotransmitter that is released into the synaptic space. Drugs like alcohol, heroin, and nicotine excite the dopamine-containing neurons in the ventral tegmental area (VTA) so that they produce more action potentials.[1,2] As the number of action potentials increases, so does the amount of dopamine released into the synapse. Amphetamines (e.g., methamphetamine, crystal, crank) actually cause the release of dopamine from the vesicles. This is independent of the rate of action potentials and, depending on dose, can cause a relatively quick and prolonged rise of extracellular dopamine levels.

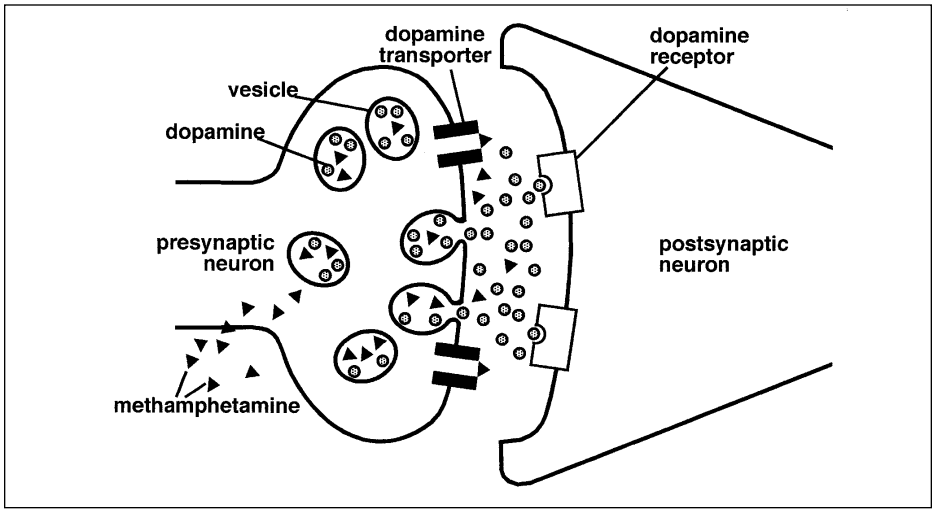


Figure 3.1: Methamphetamine alters dopamine neurotransmission in two ways. Methamphetamine enters the neuron by passing directly through nerve cell membranes. It is carried to the nerve cell terminals by transporter molecules that normally carry dopamine or norepinephrine. In the nerve terminal, methamphetamine enters the dopamine- or norepinephrine-containing vesicles and causes the release of neurotransmitter. Methamphetamine also blocks the dopamine transporter from pumping dopamine back into the transmitting neuron. Methamphetamine acts similarly to cocaine in this way.

Nicotine not only acts at the cell body in the VTA to increase the number of action potentials and number of vesicles released from a neuron, but it also acts by another mechanism to alter dopamine release. When nicotine binds to nicotine receptors on the dopamine-containing axon terminals in the nucleus accumbens, more dopamine is released with each action potential.[1]

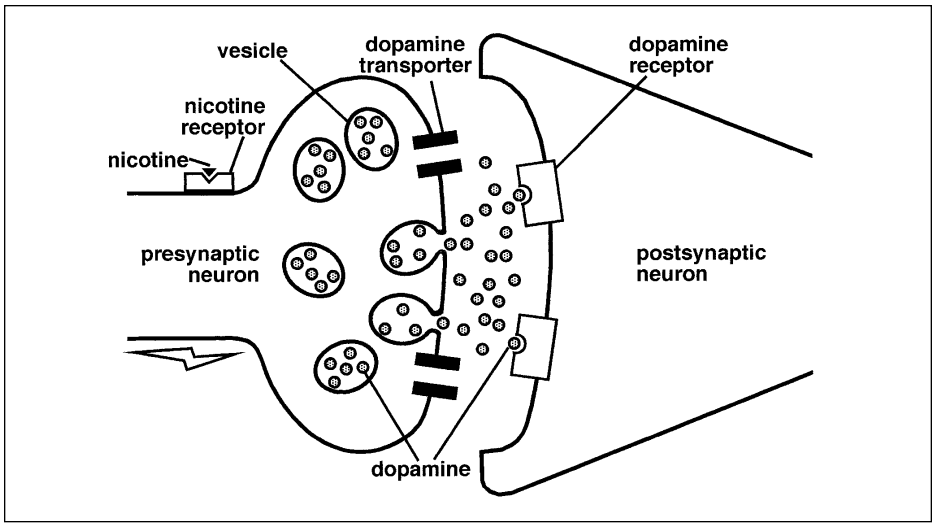


Figure 3.2: Nicotine binds to specific receptors on the presynaptic neuron. When nicotine binds to receptors at the cell body, it excites the neuron so that it fires more action potentials (electrical signals) that move toward the synapse causing more dopamine release (not shown in figure). When nicotine binds to nicotine receptors at the nerve terminal (shown above), the amount of dopamine released in response to an action potential is increased.

Drugs may also alter synaptic transmission by directly affecting the postsynaptic receptors. Some drugs activate receptors and others block them.

While THC (the main psychoactive chemical in marijuana) and morphine activate their specific receptors, other drugs block specific receptors. Caffeine, the mild stimulant found in coffee and some soft drinks, exerts its effects by preventing a neurotransmitter / neuromodulator called adenosine from binding to its receptor. Normally, the binding of adenosine to its receptor causes sedation; it is a natural sleep-inducer. Instead of causing sedation, the blocking of the adenosine receptors with caffeine leads to an increase in activity and arousal levels.[1, 3]

The actions of some drugs are very complex. LSD, for example, acts on serotonin receptors. Serotonin, an important neurotransmitter in many brain regions, is involved in regulating a wide variety of functions, including mood and basic survival functions such as sleep and eating. Scientists continue to study how hallucinogens act, but apparently LSD activates some serotonin receptors (LSD acts as a receptor agonist) and blocks other serotonin receptors (LSD acts as a receptor antagonist).[1]

A third way to affect synaptic transmission is to alter the removal of neurotransmitters from the synapse. Cocaine and amphetamines work this way (this is the second way in which amphetamines can alter neurotransmission).[1, 3] Both drugs block the dopamine transporter (reuptake pump) that removes dopamine from the synapse. The result is a fairly rapid rise of dopamine in the synapse, leading to feelings of euphoria and well-being. There are no drugs of abuse that block enzymatic destruction of neurotransmitters, although some antidepressants work by this mechanism.

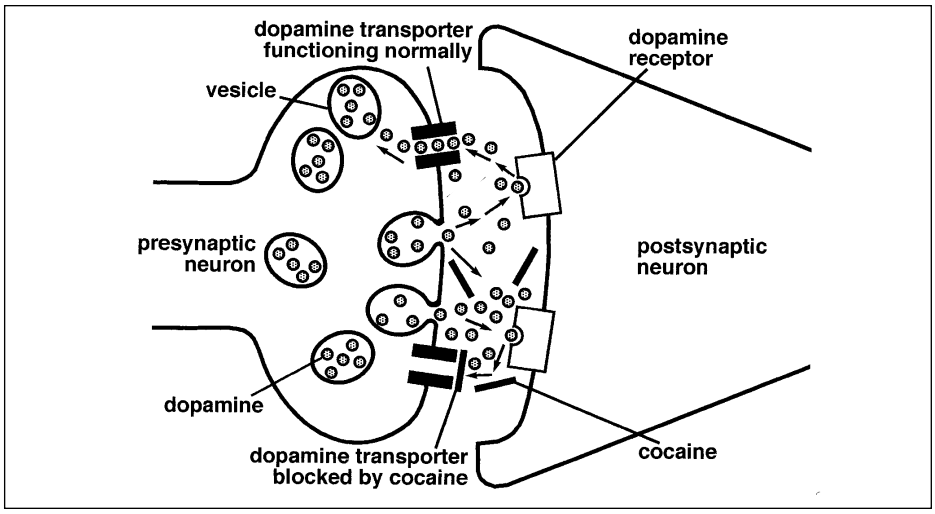


Figure 3.3: When cocaine enters the brain, it blocks the dopamine transporter from pumping dopamine back into the transmitting neuron, flooding the synapse with dopamine. This intensifies and prolongs the stimulation of receiving neurons in the brain's pleasure circuits, causing a cocaine "high."

Drugs of abuse share a common action: they act on the brain's reward system. Within that system, they all (except perhaps for LSD) share the ability to increase the levels of dopamine in the nucleus accumbens. This almost certainly accounts for the rewarding (pleasurable) effects of abused drugs.

The effects of drugs are not limited to the reward pathway in the brain. Drugs can act in various regions of the brain to exert their effects, but their ability to alter dopamine neurotransmission in the ventral tegmental area (VTA) and the nucleus accumbens is one of the most important factors that drives continued drug use.

Drugs Mimic Natural Body Chemicals

The ability of drugs to interrupt normal synaptic transmission may seem odd. After all, if receptors have such great specificity for a single type of binding partner, how can drugs disrupt the process? The answer lies in the similarity in conformation, or structure, of the drugs to natural body chemicals. For example, the receptors that bind morphine and other opiates are expressed in the brain to recognize natural opioid peptides called endorphins and enkephalins that are made by our brains and used as neurotransmitters.[4] It is an evolutionary coincidence that these receptors recognize a plant-derived chemical (drug) as well. This coincidence is a double-edged sword. Opiate compounds that come from plants are both the most potent analgesics (pain relievers) available and some of the most potent addictive drugs as well. Morphine continues to be one of the most effective drugs to relieve the pain associated with many chronic diseases. The doses of opiates used by addicts simply overwhelm the opiate receptors in the VTA and nucleus accumbens and cause profound feelings of pleasure (euphoria). Tetrahydrocannabinol (THC), the active ingredient in marijuana, binds to receptors in the brain that are specific for anandamide, an endogenous chemical that is similar in structure to THC. Because THC is similar in structure to anandamide, it binds to the same receptor. Scientists do not yet fully understand anandamide's function in the body, but it may play a role in memory functions. Marijuana disrupts short-term memory in humans. Anandamide may be involved in eliminating unneeded information from memory, but much remains to be learned before its functions are understood. Other studies indicate anandamine in an area of the brain called the dorsal striatum inhibits movements that are stimulated by dopamine.[5] This finding may enable scientists to develop medications for treating diseases such as schizophrenia, Gilles de la Tourette syndrome, or Parkinson's disease. Each of these diseases involves dopamine imbalances in the brain.

The Dose Changes the Drug's Effects

For drugs to exert their effects, a person must take them into the body and absorb them into the bloodstream. Some of these effects relate to the amount of the drug taken. For example, at low doses no effect (or response) can be observed or measured. Once a certain amount of the drug enters the bloodstream, a response can then be measured. This point is known as the **threshold**. At doses of the drug below the threshold amount, there is too little of the drug in the body to cause neurons to be activated. For example, there may not be enough heroin in the body to bind to opiate receptors in sufficient amounts to cause a change in neuronal activity. As the amount of drug taken increases, so does the response. A response cannot continue to increase infinitely, however. At some point, the response to a given amount of drug will reach a plateau, or a maximum level. To continue our example, when levels of opiates are very high in the blood, many opiate receptors have heroin bound to them and the neurons are already activated; no additional activation is possible. At higher doses, opiates are toxic and can cause a fatal response by halting respiration.

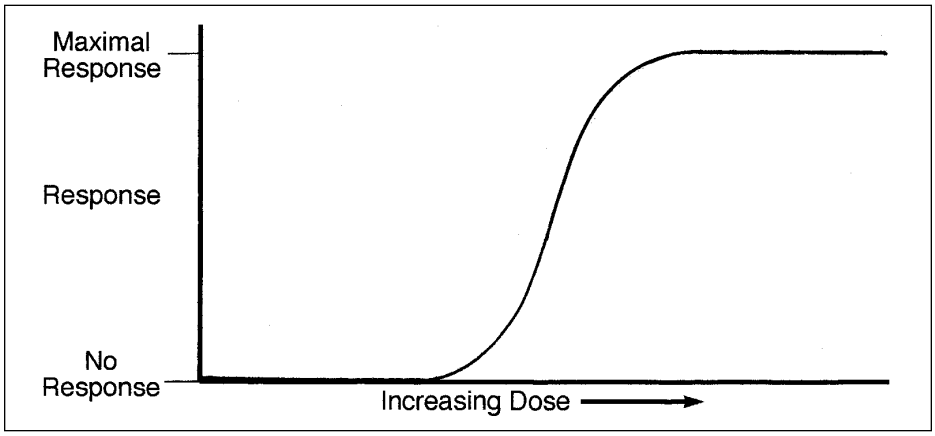


Figure 3.4: When the dose of a drug is low, no response is measurable. As the dose increases, the effect of the drug increases until it reaches a maximum. At high doses, the response to the drug remains at the maximum level.

Drugs Enter the Body in Different Ways

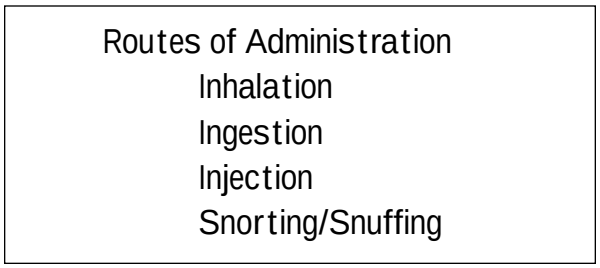


Figure 3.5: Drugs enter the bloodstream by one of four routes of administration.

The dose is not the only factor that changes the effects that a drug causes in the body. The same amount or dose of a drug can lead to milder or more severe responses depending on how the drug enters the body.[1,4] A drug that is inhaled (smoked) reaches the brain very quickly. The inhaled drugs go directly from the lungs into the left side of the heart where they enter the arterial circulation that carries them to the brain. Marijuana and nicotine are examples of drugs that are commonly taken into the body by inhalation (smoking). The intensity of the effect of inhaled drugs may be slightly less than that for injected drugs because less of the drug is taken into the body; some of the drug will be exhaled with the rest of the components of the smoke. A drug that is injected intravenously also travels quickly to the brain where it can exert its effects. The rapid passage of injected heroin, for example, brings a high risk of overdose. The heroin in the blood can reach lethal levels much faster than medical help could possibly be obtained. A third route of drug administration is by snorting or snuffing. A drug that is snorted or snuffed is taken in through the nose where it is absorbed through the mucous membranes lining the nasal passages. Television and movies often depict cocaine being snorted. The effects of drugs taken by this method will be less intense than by injection or inhalation because it takes longer for the drug to get into the bloodstream and because it does not enter the blood as efficiently. The fourth route of administration is by oral ingestion. Most people are familiar with taking a medicine, either as a solid or a liquid, by mouth. People can also take drugs of abuse this way. Drugs commonly taken orally include stimulants and depressants. Drugs taken orally enter the bloodstream more slowly than by any of the other routes. The drugs pass through the digestive tract until they reach the stomach and intestine where they are absorbed into the bloodstream. Not only do they take longer to act, but the body begins to metabolize them before they can act on the brain. Enzymes in the stomach, intestines, and liver begin breaking down the drugs so they can be cleared from the body.

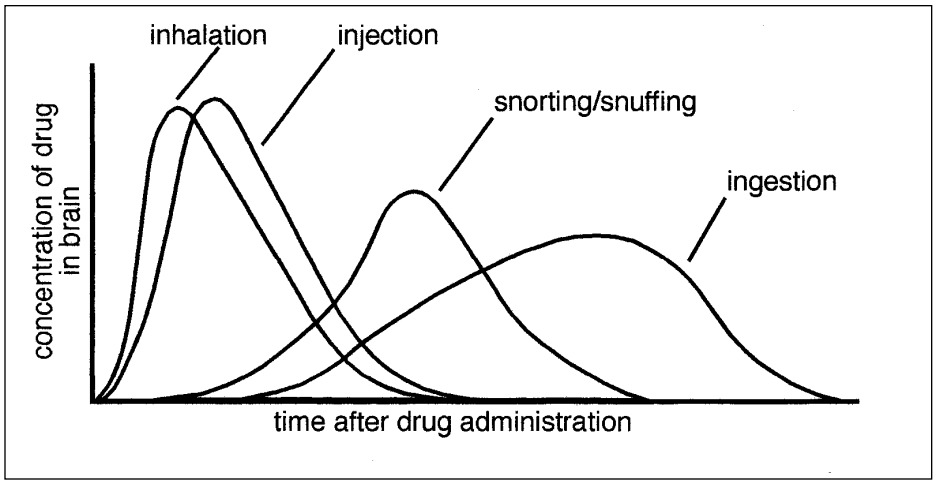


Figure 3.6: Drugs of abuse enter the body by different routes. The intensity of a drug's effect depends on how the drug is taken.

As shown on Figure 3.6, the route of administration causes dramatic differences in the onset, intensity, and duration of a drug's effect. Methamphetamine, for example, can be smoked, snorted, ingested orally, or injected. If the drug is smoked or injected, the user almost immediately experiences an intense rush or "flash" that lasts a few minutes. Snorting methamphetamine produces feelings of euphoria within three to five minutes, while oral ingestion produces effects within 15 to 20 minutes. The high resulting from snorting or ingestion is not as intense as that resulting from injection or smoking the drug.[6]

In Advance

CD-ROM Activities	
Activity Number	**CD-ROM**
Activity 1	yes
Activity 2	no
Activity 3	yes

Photocopies	
For the class	**For each student**
1 transparency of Master 3.1, *Cocaine Alters Neurotransmission* 1 transparency of Master 3.2, *Methamphetamine and Nicotine Disrupt Neurotransmission* 1 transparency of Master 3.3, *How Does Alcohol Affect Neurotransmission?* 1 transparency of Master 3.7, *What Should the Doctor Do?*	1 copy of Master 3.4, *Parent Letter* 1 copy of Master 3.5, *Caffeine: How Does Your Heart Respond?* 1 copy of Master 3.6, *How Do Drugs Get In the Body?*

Materials	
Activity 1	overhead projector computers
Activity 2	soft drinks, caffeinated and caffeine-free (see Preparation) 1 watch or classroom clock with a second hand
Activity 3	computers

Preparation

Arrange for students to have access to computers for Activities 1 and 3.

At least one week before conducting Activity 2, send a copy of Master 3.4, *Parent Letter*, home with each student to inform parents of the activity and get permission for the students to consume a caffeinated or a caffeine-free soft drink during science class. You can also use the letter to ask each student to bring in his or her own can of the designated soft drink.

Decide on a brand of soft drink that is available with and without caffeine to use in the activity. Students should drink the same brand of soft drink because each brand contains a different amount of caffeine. If students drank different brands or flavors, the results would be difficult to interpret because each student who drank a caffeinated soft drink would ingest a different dose. You will need approximately half of the students to drink a caffeinated soft drink and half the students to drink a caffeine-free soft drink. Students who do not get parental permission can participate by drinking water, thereby providing a comparison to the control group. You may obtain the necessary soft drinks through one of the following ways:

- purchase all the soft drinks yourself through your school budget,
- ask for parent or business donations to cover the cost, or
- request that each student bring in one can of soft drink, labeled with his or her name, for his or her consumption only. (If you use this approach, you will need to specify which drink each student brings to class.)

Before the day of Activity 2, have students practice taking a resting heart rate so they are used to finding their pulse, counting the beats for 15 seconds, and multiplying that number by four to get a resting heart rate for one minute (see Activity 2).

Procedure

Content Standard A: Formulate and revise scientific explanations and models using logic and evidence.
Content Standard C: Cell functions are regulated.
Content Standard C: Organisms have behavioral responses to internal changes and to external stimuli.

ACTIVITY 1: DRUGS ALTER NEUROTRANSMISSION

1. Review neurotransmission with the students. It may be helpful to have the class watch the CD-ROM animation of neurotransmission to refresh their memories. Have students refer to their summary of neurotransmission that they completed on Master 2.5.

After loading the CD-ROM on the computer, click on *Neurons, Brain Chemistry, and Neurotransmission* and then select *Neurotransmission Animation*.

2. Create a chart with the following headings on the board:

Change in neurotransmission	Effect on neurotransmitter release or availability

3. Ask students if they think there are ways that neurotransmission could be altered. As students propose ideas, fill in the chart on the board. Probe for ideas by asking questions such as:

- What would happen if certain components in the process increased or decreased in amount?
- How would that change affect the response in the responding neuron?

Students may suggest a variety of ways in which neurotransmission can be altered. For example, maybe less neurotransmitter gets released which would result in reduced (fewer) firings in the responding (postsynaptic) neuron. The postsynaptic neuron might have either more or fewer receptors; changing the number of receptors would cause an increased or decreased chance of postsynaptic neuron firing. The following chart outlines potential changes and their responses. Omit the third column on the chart at this time; you will complete that part in Step #4.

Change in neurotransmission	Effect on neurotransmitter release or availability	Drug that acts this way
increase the number of impulses	increased neurotransmitter release	nicotine alcohol* opiates*
release neurotransmitter from vesicles with or without impulses	increased neurotransmitter release	amphetamines methamphetamine
release more neurotransmitter in response to an impulse	increased neurotransmitter release	nicotine
block reuptake	more neurotransmitter present in synaptic cleft	cocaine amphetamine
produce less neurotransmitter	less neurotransmitter in synaptic cleft	probably doesn't work this way
prevent vesicles from releasing neurotransmitter	less neurotransmitter released	no drug example
block receptor with another molecule	no change in amount of neurotransmitter released, or neurotransmitter cannot bind to its receptor on postsynaptic neuron	LSD caffeine

*These drugs cause an increase in dopamine release. However, both alcohol and opiates act indirectly. See steps 10 and 11 on pages 67–68 for a more complete explanation of their actions.

4. When you have the first two columns completed on the chart, inform students that certain drugs may cause the changes in the neurons that they have suggested. Write the name of the drug next to the change as indicated in the third column on the previous chart.

Students will begin to see that drugs of abuse interfere with and disrupt the process of neurotransmission. When neurons do not communicate normally, the brain does not function normally either.

5. **Display a transparency of Master 3.1, *Cocaine Alters Neurotransmission,* showing cocaine's effect on dopamine neurotransmission. Point out that cocaine blocks the dopamine transporters. Ask the following questions:**

   • How does this blocking action of cocaine affect dopamine levels?
   • What is the effect on the responding postsynaptic neuron?

   Cocaine blocks the dopamine reuptake pumps (also called dopamine transporters). Students should recall that transporters, or reuptake pumps, carry neurotransmitter, dopamine in this case, back into the presynaptic neuron where it is repackaged into new vesicles. If the reuptake pumps cannot function, more dopamine will be present in the synaptic space where it can cause a greater stimulation of the postsynaptic neuron.

6. **After the students understand how blocking the dopamine transporters alters neurotransmission, show the CD-ROM animation on cocaine's effect on neurotransmission to the class.**

   Click *Drugs Change the Way Neurons Communicate* on the main menu and then select *How Does Cocaine Alter Neurotransmission?* to view the animation.

7. **Discuss the actions of another type of drug, methamphetamine, with the class. Display a transparency of Master 3.2, *Methamphetamine and Nicotine Disrupt Neurotransmission* (top half only). Explain that methamphetamine can act similarly to cocaine in blocking dopamine transporters (reuptake pumps). Methamphetamine also acts in another way to alter neurotransmission. Methamphetamine passes directly through the neuron cell membrane and is carried to the axon terminals. In the terminals, methamphetamine enters the vesicles that contain dopamine. This then triggers the vesicles to be released, even without an electrical signal (action potential) to cause vesicle release. Ask students how this affects the postsynaptic neuron.**

   Methamphetamine acts in two ways to change dopamine neurotransmission. Both actions lead to an increase in the amount of dopamine in the synaptic cleft. When more dopamine is present in the synaptic cleft, it is more likely to bind to the dopamine receptors on the postsynaptic neuron.

8. **Continue to assess the students' understanding of how drugs can alter neurotransmission by asking them to consider how nicotine interferes with dopamine neurotransmission in the brain. Display a transparency of Master 3.2 (bottom half). Explain that nicotine binds to receptors on the transmitting (presynaptic) neuron and causes the neuron to release more neurotransmitter each time an electrical impulse (action potential) occurs. How does this affect the activity of the postsynaptic (receiving) neuron?**

   Nicotine binds to nicotine receptors on the presynaptic neuron. The binding of nicotine to its receptor stimulates the generation of action potentials in the neuron that cause dopamine to be released from the neuron. The released dopamine can then bind to its receptor on the postsynaptic neuron. Nicotine also changes the amount of dopamine that is released. When

the presynaptic neuron fires an action potential, more dopamine is released than normal. The increased amount of dopamine in the synaptic cleft will bind to dopamine receptors on the postsynaptic neuron.

9. Display a transparency of Master 3.3, *How Does Alcohol Affect Neurotransmission?* Inform students that alcohol is an inhibitory signal and point out that alcohol acts on the dendrites of the presynaptic neuron. Ask students what other inhibitory signal they have learned.

This exercise is similar to Activity 4 in Lesson 2. Although the activity in Lesson 2 limited the signal molecules to being neurotransmitters, drugs can also be signal molecules that affect neuron activity.

Students may benefit from reviewing their work on Masters 2.7 and 2.8. Students have learned previously that GABA is an inhibitory neurotransmitter.

Now that students have expanded their understanding of neurotransmission to include how drugs of abuse can alter the process, they should be able to determine how another drug, alcohol, changes neurotransmission.

10. Ask students to use what they have learned about neurotransmission to answer the following questions:

- **How does alcohol affect the activity of the presynaptic neuron?**

Alcohol is an inhibitory signal so it reduces the activity of the presynaptic neuron.

- **If the presynaptic neuron releases GABA as its neurotransmitter, does the amount of GABA that is released increase or decrease when alcohol is present in the body?**

If the activity of the presynaptic neuron is decreased, it releases less neurotransmitter.

- **How does this affect the release of dopamine from the postsynaptic neuron?**

Because GABA is an inhibitory neurotransmitter, smaller quantities of it in the synaptic space create less inhibition of the postsynaptic neuron. Therefore, the activity of the postsynaptic neuron increases and more dopamine is released when alcohol is present.

If you complete a line for alcohol on the chart like that on Master 2.8, it would appear as follows:

Does the signal molecule excite or inhibit Neuron #1?	Does the activity of Neuron #1 increase or decrease?	Does the amount of neurotransmitter released from Neuron #1 increase or decrease?	What is the name of the neurotransmitter released from Neuron #1?	Is the neurotransmitter released from Neuron #1 excitatory or inhibitory?	Does the activity of Neuron #2 increase or decrease?	Does the amount of dopamine released from Neuron #2 increase or decrease?
inhibit	↓	↓	GABA	inhibitory	↑	↑

11. **Now that students understand how alcohol affects neurotransmission in the brain, ask them to compare how alcohol and cocaine change neurotransmission. Use the following questions to guide the discussion.**

    - **How does the way in which alcohol alters dopamine neurotransmission differ from the way in which cocaine changes dopamine neurotransmission?**

    Unlike cocaine, alcohol does not act directly on the dopamine-producing neuron. Alcohol acts on another neuron that regulates the activity of a dopamine-producing neuron. In other words, alcohol acts indirectly on dopamine neurotransmission whereas cocaine acts directly on the neuron that produces dopamine. (Opiates act by a mechanism similar to that of alcohol.)

    - **Are there any similarities in how alcohol and cocaine change neurotransmission?**

    Both alcohol and cocaine change dopamine neurotransmission and increase the amount of dopamine present in the synaptic cleft. The increased amount of dopamine increases the activity of the postsynaptic neuron.

ACTIVITY 2: HOW DOES CAFFEINE AFFECT YOU?

In Activity 1, students learned that drugs change the communication between neurons. However, hands-on classroom investigations of drugs' effects on the brain are impossible. The following activity is an exercise that students can do to learn more about how a drug, caffeine, affects their body.

Note: Before beginning this investigation, be sure to have permission forms signed by parents or guardians for the students to drink either a caffeinated or caffeine-free soft drink (use Master 3.4, *Parent Letter*). Those students who do not have permission can participate in the investigation by drinking water, thereby providing a comparison or second control for the activity.

Content Standard A: Design and conduct scientific investigations.
Content Standard A: Mathematics is essential in scientific inquiry.
Content Standard C: Organisms have behavioral responses to internal changes and to external stimuli.

1. **Several days prior to conducting Activity 2, decide which students will be in the group that drinks a caffeinated soft drink and which students will be in the group that drinks a caffeine-free soft drink. Tell students which group they will be a part of if you are asking them to bring a can of soft drink to class. Make sure students understand the need to bring only the specified type of drink.**

   Approximately half of the class should be assigned to each group. You should have permission letters specifying the type of drink for both of these groups. Any student who does not have parental permission can participate in the activity by drinking water.

2. **Because their heart rates might be elevated from their walk to class, spend several minutes allowing students to rest and talk quietly. Find out what students know about caffeine.**

   Caffeine is a mild stimulant contained in coffee and some soft drinks. People often report that mild doses of caffeine increase their alertness and

their ability to concentrate. Higher doses can cause a person to feel jittery or nervous. High doses can cause sleeplessness.

Related chemicals, theophylline (found in tea) and theobromine (found in cocoa and tea), are very mild stimulants also.

3. If you have not already done so, teach students how to find their pulse, count their heartbeats, and calculate their resting heart rate.

A student can find his or her pulse most easily by pressing two fingers against the artery in the neck or on the inside of the wrist. It is easiest to count for 15 seconds and then multiply that number by four to obtain the resting heart rate for one minute. Students should repeat the process several times until they get a consistent resting heart rate.

4. Distribute one copy of Master 3.5, *Caffeine: How Does Your Heart Respond?*, to each student. On your signal, ask students to measure their heartbeats one more time for 15 seconds, stopping when you call time. Instruct students to calculate their resting heart rate for one minute by multiplying the number they counted by four. Direct them to record it on the data table on the master.

5. Ask students to work in pairs. Distribute cans of the appropriate soft drink, one to each student. Instruct students to follow the directions on the master, and remind them to continue to sit at rest. They can talk to their partner or work on Activity 3 in this lesson, but should keep their bodies still so that they do not elevate their heart rate with activity.

6. When all the students have filled in their data tables and calculated the difference between their resting heart rate and their heart rate after drinking a soft drink, discuss their findings by asking:

- **Did your heart rate go up, down, or stay the same after you drank a caffeinated soft drink?**
- **If you drank a caffeine-free soft drink, how did your heart rate change?**
- **What happened if you drank water?**

On average, most students should have seen their heart rate go up after drinking the caffeinated soft drink. Drinking a caffeinated soft drink increased the heart rate of students in a field-test class by an average of 15 beats per minute. Drinking either a caffeine-free soft drink or water should not change the heart rate significantly.

One effect of caffeine is an increase in a person's heart rate. Scientists don't know exactly how caffeine produces its effects, but it is likely to affect the heart in two ways:

* It acts on parts of the brain that regulate the heart rate.
* It acts directly on the heart.

- **Why was it important that some students drink the same amount of a caffeine-free soft drink? Why did some students drink water?**

These questions address the need for controls in scientific investigations. Students will recognize that they are interested in determining the effect of caffeine on their heart rate. Because caffeine-free soft drinks generally contain the same ingredients as caffeinated varieties except for the caffeine, the caffeine-free soft drink serves as a control to ensure that the response is due to the caffeine in the soft drink rather than some other ingredient. Water is a second control; it ensures that the effect on the heart rate after drinking a soft drink is not caused by a different ingredient.

- **How long did the effect of caffeine last?**

Most students will find that their heart rates are either back to the resting rate or very close to it after one hour.

- **Did all the members of the class have exactly the same results when they drank a caffeinated soft drink?**

While most members of the class will see their heart rate increase, the amount of increase will vary.

- **Why do some people respond differently to caffeine than others?**

Students vary from one another in gender, size, frequency of caffeine consumption, metabolic rates, genetic makeup, and so on. This variability makes each student react differently to exposure to caffeine.

- **What could your results from the caffeine investigation tell you about how individuals respond to drugs of abuse?**

Just as individuals vary in their response to caffeine, individuals will vary in their response to drugs of abuse. The same factors: gender, body size, frequency of use (development of tolerance), genetics, and the individual's metabolic rate will influence a person's response.

7. **If you are conducting this activity in several classes, you may wish to pool the data from all classes to have a larger sample size.**

8. **Discuss the last item on the master that asks students to consider how different doses of caffeine might affect the response. Encourage students to design an experiment to investigate this.**

   Students likely will propose that drinking a small amount of soft drink will cause only a slight increase, if any, in a person's heart rate, while drinking a large volume of soft drink will cause a larger increase in heart rate. This leads students to consider the concept of dose.

   To investigate the effect of dose on the body's response to caffeine, students may propose that different groups of students drink different amounts of caffeinated soft drink. For example, students could drink 1 ounce, 2 ounces, 4 ounces, 8 ounces, or 16 ounces of soft drink. The design should include appropriate controls. Caffeine-free soft drink again could serve as the control if it were consumed in equal amounts to the caffeinated variety.

Many soft drinks popular among youth contain caffeine. The accompanying table lists some soft drinks (12-ounce size) and the amounts of caffeine they contain.

Compared with other caffeinated drinks popular with adults, the caffeine content in soft drinks is lower. Coffee can contain between 80 and 175 milligrams of caffeine (per seven ounces) depending on how it is brewed; espresso has 100 milligrams in just 1.5 to 2.0 ounces. Tea can contain 40-60 milligrams of caffeine (per seven ounces). Ice tea contains 70 milligrams of caffeine in 12 ounces.

Caffeine in Soft Drinks

Soft Drink	Milligrams in 12 ounces
Jolt Cola	71 mg
Josta	58 mg
Mountain Dew	55 mg
Surge	51 mg
Diet Coke	45 mg
Coca-Cola	45 mg
Dr Pepper	41 mg
Sunkist Orange Soda	40 mg
Pepsi Cola	37 mg
Barqs Root Beer	23 mg
7-Up	0 mg
Minute Maid Orange Soda	0 mg
Mug Root Beer	0 mg

Source: Center for Science in the Public Interest. Soft drinks and health: Caffeine content of foods and drugs. Retrieved August 17, 2000 from the World Wide Web: *www.cspinet.org/new/cafchart.htm.*

ACTIVITY 3: ROUTES OF ADMINISTRATION

1. Give students the opportunity to view the CD-ROM segment, *Paths to the Brain.*

After loading the CD-ROM on the computers, pull up the main menu. Click on *Drugs Change the Way Neurons Communicate* and then select *Pathways to the Brain*.

Content Standard A: Communicate and defend a scientific argument.

2. Give each student a copy of Master 3.6, *How Do Drugs Get In the Body?* Students may work in groups of three to analyze the graph and answer the questions.

Note to Teachers: The graph shown on Master 3.6 is a generalized representation of the speed and intensity of response to drugs. Very few, if any, drugs are commonly taken by all of the different routes.

SAMPLE ANSWERS TO QUESTIONS ON MASTER 3.6

Question 1. Four drug abusers each take a drug. One person injects 100 milligrams of a drug into a vein, one person smokes 100 milligrams of the drug, one person snorts 100 milligrams of the drug, and one person swal-

lows or ingests 100 milligrams of the drug. Who will experience the greatest effect of the drug? The individual with the greatest concentration of drug in the brain will have the greatest effect.

The graph indicates that the individuals who inhale the drug or inject the drug into a vein will experience the greatest effect from the drug. These individuals will have a higher concentration of the drug in the brain than the people who snort (absorption through the mucous membranes) or ingest the drug. The concentration of drug in the brain will be slightly lower for inhalation than injection because some of the smoked drug is exhaled in the smoke.

Question 2. Who will experience the quickest effect from the drug?

The person who inhales the drug will experience the quickest effect from the drug (assuming the person inhales the whole 100 mg). The inhaled drug goes directly into the left side of the heart and then enters the arterial circulation to the brain, while injected drugs enter the venous circulation that returns the blood to the right side of the heart. The drug that enters the venous system takes longer to exert its effect because the blood must go to the lungs and then to the left side of the heart before it is pumped to the brain and the rest of the body.

Question 3. Who will experience the least effect from the drug?

The person who ingests, or swallows, the drug will experience the least effect.

Question 4. Who will experience the slowest effect from the drug?

The person who ingests, or swallows, the drug will also have the slowest effect.

Question 5. Tobacco smokers can use nicotine patches to help them quit smoking. The nicotine patches help the smoker slowly lower the amount of nicotine that enters the body. How does the nicotine in the patch enter the body?

Nicotine would enter the body by absorption through the skin.

Question 6. Explain why the different ways of taking drugs cause different responses.

Taking drugs by inhalation causes a very rapid increase in the level of drug in the brain. Inhaled drugs are absorbed into the arterial bloodstream in the lungs and then pumped to all parts of the body including the brain. Taking drugs by intravenous (IV) injection also causes a rapid increase in the drug level in the brain. It is slightly slower than inhalation because the drug goes first to the right side of the heart, is then pumped to the lungs where the blood is oxygenated, then goes back to the left side of the heart, and finally to the brain and body. Absorption through the skin or mucous membranes would be slower yet because the drug has a longer path to

travel before being circulated throughout the body. Drug response would be the slowest after ingestion because the drug goes into the digestive tract and then must pass through the walls of the stomach and intestine to enter the blood capillaries.

3. Display a transparency of Master 3.7, *What Should the Doctor Do?* Discuss the reasons why one action may be more appropriate than others.

Based upon what you have learned about how drugs act in the body, how should morphine be given to the patient? Should the morphine be given as a pill, as a shot, or as an inhalant? Consider each alternative and explain why the different methods should or should not be chosen.

If students understand that taking drugs into the body by different routes causes different responses, they should be able to explain that the different ways of administering drugs can have advantages and disadvantages. Use this scenario to evaluate students' understanding.

The question concerning how morphine should be administered to a patient to relieve pain is designed to assess if students understand how different ways of getting drugs into the body changes their effects. The doctor's goal is to relieve the patient's pain quickly so that the fracture can be set.

Based on the graph that students analyzed on Master 3.6, the doctor should elect to give morphine as an inhalant or an injection. In each case, the drug reaches the brain quickly. Inhaled drugs may reach the brain even faster than injected drugs. Perhaps the main disadvantage of giving the morphine as an inhaled drug is the amount of drug that actually enters the bloodstream is more variable. After inhaling the drug, the person exhales; some of the drug is carried out of the body during the exhalation. If the drug is injected, all of the drug is delivered into the bloodstream. The doctor knows how much morphine enters the bloodstream. Giving a pill to the patient would be less effective than the other means for pain relief because it would take longer for the drug to act and its concentration in the bloodstream would be lower.